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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,438	12/03/2001	Liming Yu	TNX95-02ABB	8540
26839	7590	11/14/2005	EXAMINER	
TANOX, INC. 10301 STELLA LINK HOUSTON, TX 77025			CHANDRA, GYAN	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,438	YU ET AL.	
	Examiner	Art Unit	
	Gyan Chandra	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-22 is/are pending in the application.
- 4a) Of the above claim(s) 17 and 20-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14-16, 18 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>8/25/2005</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The amendment of claim 16 has been made of record. Claims 14-22 are pending and claims 17, 20-22 are withdrawn from further consideration as being drawn to a non elected invention.

Claims 14-16 and 18-19 are under examination.

The text of those sections of Title 35, U.S. code not included in this action can be found in a prior Office Action.

Election/Restrictions Requirement:

Applicants argue that claim 17 does not impose any additional search burden because there is no additional sequence search is involved. Further they argue that Groups III and IV (Group 3 and 4 as of records of Office Action 10/28/2004) should be included with present examination.

Restriction requirement, mailed on 10/28/2004, is a Linking restriction which states that claim 14 links Groups 1-4 and upon allowance of linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

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Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The crossed references are missing from the previously submitted copies of references. Applicants may, in response to this and no later Office Action, submit the missing references. Such submissions will be considered to have been part of the respective Information Disclosure Statement filed on 12/3/2001, and the PTO-1449 will be updated accordingly. No fee for the submission of such references is required, nor should applicants file an additional form PTO-1449 with the missing references.

Priority

In view of Applicant's Remarks filed on 8/25/2005, the instant Application gets priority of 3/16/1999.

Response to Arguments

Objection/Rejections - withdrawn

Rejections - 35 USC § 112-second paragraph

The rejection of claim 16 under for being indefinite in that it recites acronyms such as ADCC, is withdrawn due to the amendment of claim 16 by providing scientific term of the recited acronym.

Objection/Rejections - maintained

Double Patenting

Applicants point that U.S. Patent No. 5,727,125 is not Applicant's patent. It was a typographical error as pointed in the response and the correct U.S. Patent No. is 5,723,125 (which has been incorporated in by reference on page 6, under Example I of the specification). Therefore, the Double Patenting rejection is maintained for the reasons of record in the previous Office Action mailed on 4/25/2005.

Claims 14 -16, and 18-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,723,125 in view of Peterhans et al (IDS, Analytical Bioch. 163:470-475, 1987). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims are drawn to a hybrid molecule comprising an interferon molecule joined to its C-terminal end through a peptide linker to the N-terminal of a first gamma immunoglobulin Fc fragment. The instant application claims an IFN-Fc hybrid molecule comprising an interferon molecule joined at one end to one chain of an immunoglobulin Fc fragment without any linker.

Peterhans et al teach a human interferon alpha2/beta galactosidase hybrid molecule wherein beta galactosidase is fused to the C-terminus of interferon alpha2 establishing the making of functional interferon C-terminal hybrid molecule. It would have been prima facie obvious to one of ordinary skill in the art to make an interferon/Fc gamma chain fragment hybrid molecule of US Patent 5,723,125 without using a linker as taught by Peterhans et al. One of ordinary skill in the art would have

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been motivated to make a hybrid IFN-Fc without linker because it is easier to make a direct fusion of proteins as taught by Peterhans et al.

Claim Rejections - 35 USC § 112-written description

The rejection of claims 14 -16, and 18-19 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained for reasons of records.

Claims 14-16 and 18-19 are drawn to an IFN-Fc hybrid molecule comprising an interferon molecule joined at one end to one chain of an immunoglobulin Fc fragment without any linker between the interferon and the immunoglobulin Fc fragment, and functional IFN-Fc variants thereof.

Applicants argue that even though they have disclosed a single species and it includes a functional language requirement and the specification provides a method to test the functionality as recited in Example II. Therefore, this meets written description requirement.

Applicants' arguments have been fully considered but they are not found to be persuasive. The factors to be considered include disclosure of complete functional characteristics, function correlation, method of making an invention, method of treatment, or any combination thereof. The instant application discloses that a linker of different length from one amino acid to 16 amino acid can be used to attach the C-terminus of interferon with N-terminus of immunoglobulin Fc. Applicants do not provide a definition of "a variant" or disclose any IFN-Fc variant, if they had at the time of filing of the instant application. As such IFN-Fc variants encompasses a huge number of

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substitutions, insertions, deletions, and mutations. Thus, the claims are drawn to a genus of IFN-Fc hybrids. The skilled artisan cannot envision the detailed underlying mode of making innumerable variants of IFN-Fc hybrid, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of achieving it.

Claim Rejections - 35 USC § 112-enablement

The rejection of claims 14 -16, and 18-19 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for functional IFN-Fc variants, is maintained for the reasons of record in the previous Office Action mailed on 4/2/5/2005.

Claims are drawn to a genus of IFN-Fc variants.

Applicants argue that they have claimed "functional variants" and have support for testing a variant in a test assay.

Applicants' arguments have been fully considered but they are not found to be persuasive. The specification does not disclose variants of IFN-Fc and residues within IFN-Fc that are required for functional variants. As such making innumerable mutations, deletions, insertions to achieve functional variants, and testing these for achieving functional variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 103

The rejection of claims 14-16 and 18-19 under 35 U.S.C. 103(a) as being unpatentable over Landolfi (IDS, U.S. Patent 5, 349,053) in view of Frencke (IDS, EP

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467416) or Peterhans et al (IDS, Analytical Bioch. 163:470-475, 1987) is maintained for reasons of records.

Claims are drawn to an IFN-Fc hybrid molecule comprising an interferon molecule joined at one end to one chain of an immunoglobulin Fc fragment without any linker between the interferon and the immunoglobulin Fc fragment and functional IFN-FC variants wherein (i) gamma-4 chain Fc fragment does not induce ADCC, (ii) the interferon molecule is interferon α 2a or interferon α 2b and (iii) a composition comprising the hybrid.

Applicants argue that the reference Landolfi or peterhans et al do not suggest combining the references and that there is no reasonable expectation of success. Applicant states that even though reference EP467416 disclose that interferon complex increases half life, one skill of art would not look at it because it is an antigen –antibody complex. Further, Applicants argue that Peterhans reference teaches fusion of human interferon alpha2/beta galactosidase hybrid molecule, one would not think in the direction of increasing half-life of a fusion protein.

Applicant's arguments have been fully considered but they are not found to be persuasive because Landolfi teaches "chimeric molecules that comprises a portion of a ligand molecule linked to the constant region of an immunoglobulin molecule" (column 4, lines 10-13) wherein the Fc region is a human gamma heavy chain (column 6, lines 51-59). Landolfi also examined IgG mediated ADCC and suggests that the antibody dependent cell toxicity (ADCC), resides in the Ig constant region (column 14, lines 64 - 68). Peterhans teaches how to make a fusion protein. The reference EP467419 teaches

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that interferon α -antibody complexes make the IFN α more stable and desirable for in vivo use. Therefore, it would have been prima facie obvious to one of ordinary skill in the art to substitute interferon/Fc gamma chain fragment hybrid molecule of Landolfi with interferon α as taught by Frincke to make a hybrid molecule or a fusion protein as taught by Peterhans with a reasonable expectation of success.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1646
03 November 2005
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JANET L. ANDRIES
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